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**Remarks/Arguments**

Claims 1, 14, and 15 have been amended as indicated. Support for the claims as amended is found throughout the specification. For example, the sequences recited in claims 14 and 15 are described in Examples 17, 18, 24, and 25. Support for a compound comprising 8-consecutive nucleobases of an illustrated compound is found on page 14. No new matter is introduced by these amendments.

Applicants have cancelled claims 16-18 without prejudice. Applicants have also cancelled claim 38 without prejudice. Applicants reserve the right to prosecute the cancelled claims in a continuing application filed during the pendency of the present application.

The Examiner has restricted the pending claims into the following groups:

Group I: Claims 1-29, drawn to a compound 8 to 80 nucleobases in length targeted to a gene encoding forkhead O1A, classifiable in class 536, subclass 24.5.

Group II: Claims 30-37, drawn to a method of inhibiting the expression of forkhead box O1A and a method of treating an animal having a disease or condition associated with forkhead box O1A, classifiable in class 435, subclass 6 and 375.

Group III: Claim 38, drawn to a method of screening for a modulator of forkhead box O1A, classifiable in class 435, subclass 6.

Group IV: Claims 39-41, drawn to a method of decreasing blood or plasma glucose, improving glucose tolerance, and normalizing insulin levels comprising administering a compound targeted to forkhead box O1A, classifiable in class 435, subclass 6.

Applicants elect group I with traverse.

The Examiner has further required restriction within Claims 14-18, stating that the Applicants are entitled only to the examination of a single sequence. With respect to

restriction within Claims 14-18, Applicants traverse. While the Examiner acknowledges that all of the sequences listed in Claims 14-18 are related as oligonucleotides which all target the same gene, the Examiner states that each sequence is considered to be unrelated.

As explained in MPEP Section 803.2, the USPTO cannot refuse to examine that which applicants deem to be their invention unless the subject matter lacks unity of invention. *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 198 USPQ 334 (CCPA 1978), unity of invention exists where components in a Markush group share common utility and share a substantial structural feature disclosed as being essential to that utility. *In re Harnisch* 206 USPQ 300 (CCPA 1980). In *Harnisch*, the court reversed a rejection of a claim to a group of coumarin compounds, stating that the compounds were structurally similar and functionally similar because all were dyestuffs, which was not repugnant to scientific classification. Like in *Harnisch*, all of the compounds are structurally similar (i.e., they are oligomeric compounds) and are functionally similar (i.e., inhibit forkhead box O1A). Furthermore, oligomeric compounds are not repugnant to scientific classification.

The Examiner states that the compounds are not structurally similar because each has a unique sequence. With all due respect, this is not the appropriate standard. By definition, each member of any genus will have a structural distinction. In the case of coumarins, it will be one or more chemical substituents pendant from a coumarin backbone. In the case of oligonucleotides, the distinction will often be the "sequence." Antisense compounds belong to a recognized scientific class of compounds. For all the reasons that the coumarin species in *Harnisch* possessed are structurally similar, the antisense compounds of the present claim are structurally similar. Thus, the Patent Office's burden is not satisfied by observing that each member of a genus was not identical.

The Patent Office's restriction practices in oligomeric compound applications are arbitrary and capricious, as evidenced by the practices adopted in other technical areas. The practice creates an undue burden upon applicants that develop oligomeric compounds, requiring the filing of hundreds or thousands of applications to protect a single inventive concept, a practice that is not imposed upon other technologies. For example, antibodies, like antisense compounds, are compounds that inhibit the function

of a target. The Patent Office routinely grants antibody claims that are defined by the target. See, for example, US Patent No. 6,921,645 and the patent application at issue in *In re Wants*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). Antibodies, like oligonucleotide sequences, differ from one another in their specific sequences and possess different epitopic specificity (i.e., they bind to different regions of the target molecule). However, the Patent Office routinely examines claims directed to antibodies to a given target without burdening an Applicant with the necessity to file a divisional on each and every individual species. Likewise, the Patent Office routinely allows a patent applicant to claim a gene and fragments thereof. Like antisense compounds, fragments of a gene individually possess different sequences and all possess a common function as, for example, primers to isolate the gene. However, the Patent Office routinely examines claims directed to genes and fragments thereof without burdening an Applicant with the necessity to file a divisional on each and every individual species. See, for example, US Patent No. 6,924,134. A quick review of patents granted by the Patent Office in these areas of biotechnology establishes that this restriction requirement is contrary to accepted practice.

The Examiner asserts that searching the individual species in this case is burdensome. The most relevant search for the claimed inventions is a search of the target sequence as the antisense oligonucleotides are all related in their sequence to the target sequence. Thus, a search of a single sequence, provided that the proper search rationale is employed, can be performed.

Applicants elect SEQ ID NO: 172 with traverse. Withdrawal of the restriction is respectfully requested in light of the above arguments.

The Examiner states that Groups I and II are properly restricted pursuant to MPEP 806.05(h) because the products of Group I are useful in a materially different process, citing a hybridization assay for determining tissue-specific gene expression. The example provided by the Examiner does not state the methodology that would be employed in the assay. The Examiner further states that a search of both the product and methods of using the product for inhibiting gene expression is a burden and that the subject matter is divergent and non-coextensive. Applicants disagree.

Claim 1 is linked to Claims 30-37 as they require the Examiner to consider the ability of the compound to inhibit forkhead box O1A expression. The sequences of the compounds in Claims 1 and 30-37 are the same and thus, the search will be the same. It is respectfully requested that the restriction requirement between Groups I and II be withdrawn.

Likewise, the Examiner states that Groups I and IV are properly restricted pursuant to MPEP 806.05(h) because the products of Group I are useful in a materially different process, again citing a hybridization assay. The Examiner also states that the restriction is proper because the subject matter is divergent and non-coextensive and a search for one would not necessarily reveal art against the other. Applicants disagree. As with the claims of Group II, the claims of Group IV require the Examiner to consider the ability of the compounds to decrease forkhead box O1A expression. The sequences of the compounds in Claims 1 and 39-41 are the same and thus, the search will be the same. It is respectfully requested that the restriction requirement between Groups I and IV be withdrawn.

Furthermore, the Examiner asserts that the inventions of Groups II and IV are unrelated. Applicants traverse. The different methods disclosed in Groups II and IV, are, in fact, related, in that both require decreasing forkhead box O1A. The Examiner further asserts that the subject matter is divergent and non-coextensive, and thus the search presents a burden. As discussed above, the Applicants assert that the sequences of the compounds in Group II and Group IV are the same and, thus, the search will be the same. The placement of inventions of both Group II and Group IV into identical classes and subclasses (class 435, subclass 6) supports this assertion. It is respectfully requested that the restriction requirement between Group II and Group IV be withdrawn.

Applicants thank the Examiner for indicating that if the elected product claim is found allowable, the process claims depending from or including all of the limitations of the product claim will be entered and examined. Claims 30 to 37 incorporate all of the limitations of Claim 1. Thus, if the restriction requirement is maintained, Applicants request that rejoinder of the claims in Group II be considered upon allowance of Group I. Likewise, Claims 39 to 41 incorporate all of the limitations of Claim 1. Thus if the

restriction requirement is maintained, Applicants request that rejoinder of the claims in Group IV be considered upon allowance of Group I.

Applicants reserve the right to prosecute any non-elected subject matter in a continuing application filed during the pendency of the present application.

**Fees and Petition Under 37 CFR 1.136(a)**

The Applicants herewith petition for a one-month extension of the time to reply to the Office action dated October 24, 2005. The fee required should be charged to Isis Pharmaceuticals, Inc. as small entity status, Deposit Account 50-0252, referencing attorney docket number HTS-0008US.P1

It is believed that no other fee is due with this response. However, if additional fees are due, the Commissioner is hereby authorized to charge the fees to the above-numbered deposit account as small entity, referencing attorney docket number HTS-0008US.P1

**Conclusion**

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, an early office action on the merits of this case is respectfully requested.

Respectfully submitted,

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